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## (54) Nutritional and medicinal compositions

(57) Compositions in the form of an emulsion or a paste containing polyunsaturated oil providing at least one essential polyunsaturated fatty acid and dietary fibre in the form of for example leguminous seeds containing a phospholipid emulsifying agent, root vegetables and gums have been found to produce a palatable dietary supplement. A leguminous seed may act as emulsifying agent for a fish oil in a supplement for correcting relative dietary deficiency of polyunsaturated fatty acids (PUFAs) of the omega-3 and omega-6 series, and the also provides dietary fibre. The palatability of the presentation enhances patient acceptability and compliance.

The compositions may be in dose packs or in resealable containers.

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Nutritional and Medicinal Compositions

This invention relates to Nutritional and Medicinal Compositions, and in particular to compositions containing certain essential polyunsaturated fatty acids (present in marine lipids and vegetable oils) and vegetable fibre. The invention provides a nutritional supplement providing these components of diet which are essential for healthy function, in a palatable form. The intake of essential fatty acids (EFA) is dependent on cultural factors, tolerability of foods rich in EFAs and dietary preference.

The principal fats in diet are mono-, di- but mainly tri-glycerides of fatty acids. The constituent fatty acids may be saturated, monounsaturated or polyunsaturated, for example palmitic and stearic acid are saturated fatty acids which have carbon chains of 16 and 18 atoms, respectively. Mono-unsaturated fatty acids such as oleic acid, cetooleic and gadoleic acids all have carbon chains of 18 atoms.

Polyunsaturated fatty acids (PUFAs) have at least 2 pairs of unsaturated-C-C-bonds. PUFAs such as linoleic and linolenic acid are obtained from vegetable oils. Eicosapentaenoic (EPA) and docosahexaenoic (DHA) acids, which are characteristically obtained from marine lipids, cannot be synthesised by man.

Lipids have roughly equivalent energy content when metabolised in the body. However, PUFAs have other functions which are dependent on their ability to enter into a cascade of chemical reactions in the body. PUFAs are precursors of pharmacologically active substances and also enter into the structure of nerve and other cell membrane lipids. Certain PUFAs are referred to as being 'essential'. Essential fatty acids can be characterised by the number of carbon atoms in the chain, the number of double bonds and the position of the first double bond in relation to the methyl (omega or n) end of the chain. For example, EPA is 20:5 w-3, alpha ( $\alpha$ )-linolenic acid is 18:3 w3 and gamma ( ) linolenic acid is 18:3 w-6.

The benefit of fish oils as therapeutic agents and also as dietary supplements is described in many original papers and is summarised in texts such as "Seafoods and fish oils in human health and disease" by Kinsella, JE (Marcel Dekker Inc.), 1987.

The beneficial effects of fish oil and/or oily fish consumption are well documented and their use in moderate dosage carries low risk. The content of w-3 PUFAs in fish is variable not only between species but also in the same variety of fish at different seasons of the year. Standardised fish oils provide PUFA supplementation at a lower cost in terms of calories and cholesterol but are unpleasant to take.

Man is therefore dependent on supply of EPA and DHA from marine lipids. The daily requirement of essential fatty acids and hence the amount which needs to be added as a supplement cannot be defined exactly for any one individual. Westernised diets may contain less than 0.3g of w-3 PUFAs and it has been estimated that the amount required for the maintenance of normal health is between 1 and 2g of w-3 PUFAs per day. From the diet this could be provided by a portion of approximately 150g of salmon or approximately 750g of cod. Not everyone has access to whole fish, and some individuals have an aversion or allergy to fish, particularly oily fish which contains a high proportion of the w-3 PUFAs. Additionally, some types of whole fish contain long chain (C20 and C22) mono-enoic fatty acids which are not essential and are reported to have an adverse effect on heart muscle.

The effects of long chain monoenoic acids should be distinguished from the wholly beneficial effects of oleic acid. Oleic acid (18:1 w9) is a monounsaturated acid which is obtained from diet and is also produced in the body from stearic acid. It has less antihypercholesterolaemic activity than polyunsaturated fatty acids and is non toxic. Longer chain monoenoic acids such as gadoleic, cetoleic and erucic acid which are present in fish can produce cardiac lipidosis. Humans quickly adapt to metabolic long chain monoenoic fatty acids but a high concentration of monoenes is considered undesirable and is reduced during the refining of fish oils intended for use as dietary supplements. The content of long chain monoenoic acids in vegetable oils is limited by legislation.

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Prepared blends of fish oils have a low content of long chain monoenes, and these specially selected fish oils are the source of w3 PUFAs in the compositions described herein.

Vegetable oils such as Evening Primrose Oil contain relatively large amount of gamma ( $\gamma$ )-linolenic acid (w-6); oils from certain leaves contain small quantities of alpha ( $\alpha$ )-linolenic acid (w3). Supplementation with these oils is normally at the rate of 100-600mg PUFA per day.

Fatty acids of the w-3 series occur in small amounts in meat from animals fed a diet containing fish meal but very small amounts when fed a non-fish containing diet. They are present in only low concentrations in vegetable oils. Man can convert some saturated fatty acids into the polyunsaturated acids of the w- 3 series but this is done with very low efficiency and is not a reliable source of w- 3 PUFA's.

There are various pharmaceutical preparations based on marine lipid which are intended to provide the amounts of EPA and DHA which are necessary to produce a therapeutic effect. These include salmon oil, sardine oil, cod liver oil and refined, blended marine lipids. The usual methods of administration are as the oil, which may be flavoured, or as oil contained in soft gelatin capsules. It is generally recognised that for therapeutic purposes a daily quantity of 10g (11 ml) of oil containing 1.8g of EPA in total should be given in divided doses. In some trials the dose has been twice this figure. The oil has a more or less pronounced "fishy" odour and taste which is difficult to conceal, and this may lead to problems of consumer compliance. The corresponding dose given in capsules involves the administration of 10 capsules each containing 1 g of oil per day and again this is an inconvenient method of administration.

When marine lipid is given as a dietary supplement with the object of maintaining good health, smaller quantities of marine lipid are required and consumer compliance can be ensured by presentation of marine lipid in an attractive and palatable formulation.

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There is therefore a need for a product to provide supplementary essential fatty acids, particularly EPA and DHA in a form which will ensure patient compliance. The oils are not pleasant to take, and attempts to disguise the characteristic taste, and search for a suitable vehicle led to the surprising discovery that pulps prepared from leguminous seeds and root vegetables have good taste masking properties and also provide vegetable fibre.

According to this invention there is provided a composition containing a polyunsaturated edible oil, ie fish oil and/or a vegetable oil and a dietary fibre in homogeneous mixture which is intended as a nutritional supplement. The composition is provided in a unit dose presentation in an attractive, palatable form which will encourage patient compliance. The dose unit is of such a size as to provide a proportion of the daily requirement of the essential PUFAs and vegetable fibre.

Essential fatty acids from vegetable sources, particularly linoleic and linolenic acids, and the products of their metabolism have been shown to reduce plasma cholesterol levels. This hypcholesterolaemic effect is exerted by a mechanism which is different from that involved in the sequestration of bile acids by dietary fibre and the effects are additive.

It is also known that an adequate intake of vegetable fibre can, in addition to its beneficial bulking effect in the gastro-intestinal tract, also lower plasma cholesterol by retaining or sequestering cholesterol within the content of the bowel, thus preventing reabsorption. Activated charcoal has a similar adsorbant effect. Fibre, also commonly referred to as dietary fibre, is the part of vegetable-derived food that passes through the small intestine undigested and reaches the large intestine largely intact. Dietary fibre consists of lignin, cellulose and polysaccharides, hemicelluloses and gums; the proportion of each component varies according to the vegetable source. The outer skin of cereal grains (bran) is a source of dietary fibre and can be used in this invention. However a source of ditary fibre which contains a low content of phytic acid (which sequesters calcium) and a greater proportion of hemicellulose and pectin, such as bean or beet fibre, is preferred.

In this invention the starting material is typically dried lentils, yellow split peas, green split peas, chick peas, haricot beans, soya beans, defatted soya bean powder, chick pea powder, butter beans and other seeds of the family leguminosae herein after referred to as "beans". The fresh or dried beans can be hydrated by cooking but preferably are first soaked in water, or water containing a softening agent which may be an alkali metal, carbonate, bicarbonate, pyrophosphate or a combination of these agents. Use of softening agents produces a product with a higher pH value than water alone and during subsequent cooking the pH may rise. The high pH produced in this way has been found to be beneficial in the production of oil-in-water emulsions. Adjustment of pH to improve palatability and enhance the stability of the final product can be made with an organic fruit such as acetic, ascorbic, citric, tartaric or malic acid or an inorganic acid such as hydrochloric or sulphuric acid.

Investigation of emulsifying agents which can be used to produce an emulsion of fish oil and thereby improve its palatability include an examination of plant gums and lecithins.

An unexpected finding was that leguminous seeds which are known to be rich in lecithin, or a mixture of such seeds with root vegetables and/or nuts can be prepared so that they act as emulsifiers for oils rich in w-3 and w-6 PUFAs. Additionally they yield a high amount of soluble fibre. Furthermore, heat treatment of the seeds of leguminous plants provides a bland base which helps to mask the fishy taste of the marine lipid oil. The vegetable base thus provides both fibre and emulsifying agent.

Emulsions of fish oil may also be produced by the use of purified lecithin from vegetable sources, milk lecithin or extracts of egg yolk. The term "lecithin" is used commercially to describe specifically phosphatidyl choline and also a mixture of phosphatidyl choline and phosphatidyl ethanolamine together with other phospholipids. Naturally occurring or purified lecithin from sources other than leguminous seeds can be used in combination with vegetable fibre to produce an emulsified fish paste.

The invention can also be used to prepare palatable formulations where the oil and lecithin are both derived from a solvent extract of egg yolk or soybean such as compound AL 721 described

in US patent 4,474,773 and EP 0074251.

Vegetable gums can be used to stabilise emulsions produced by means of lecithin, and the incorporation of a small amount of a water soluble gum such as guar gum, xanthan gum or methyl cellulose can be used to modify the texture of the product and also to make a small contribution to the total amount of dietary fibre contained in the preparation.

The nutritional composition contains a proportion of fish oil which may be adjusted to accommodate the variable content of EPA and DHA in commercial fish oils. The nutritional composition may contain from 0.25g to 5.0g of EPA and 0.5 to 20g of dietary fibre per portion or serving of 15-250g. The composition may preferably contain 0.6 - 3.6g of EPA and 2.0 - 5g of dietary fibre per serving of preferably 30-100g.

The compositions of the invention are intended for oral administration as a dietary supplement and may be in the form of an emulsion or homogenous paste having a pH of between 2.5 and 6. The invention also includes the use of flavouring agents. With aqueous compositions, which are susceptible to contamination and subsequent deterioration by micro-organisms it is preferable to include an anti-microbial preservative. A suitable system is a combination of agents which are approved for this purpose including a combination of methyl- and propyl- p-hydroxybenzoates or their sodium salts, benzoic acid or its sodium salts, sorbic acid or its potassium salt, sodium metabisulphite or a mixture thereof.

Polyunsaturated fatty acids are susceptible to oxidation and it is preferable to incorporate an antioxidant in the formulations. Suitable antioxidant are those which are approved for use in food and include ascorbic acid and its esters, tocopherols, propyl gallate, octyl gallate, dodecyl gallate, butylated hydroxyanisole, butylated hydroxytoluene, and ethoxyquin or a mixture thereof. Oxidation can also be minimised by substantially removing entrained air from the product and flushing with an inert gas, preferably nitrogen, before sealing the product into packages. The composition of the present invention may also include one or more of a colouring, sweetening or flavouring agent.

The invention is illustrated by the following examples.

Examples 1 to 4

Quantities in grams unless otherwise stated, batch size approximately 300 g.

|                                 | 1     | 2     | 3     | 4     |
|---------------------------------|-------|-------|-------|-------|
| Chick peas (Cooked weight)      | 110   | 100   | 110   | 100   |
| Egg Yolk                        | -     | 7     | 5     | -     |
| Smoke Powder (flavouring agent) | 10    | 10    | -     | 10    |
| Onion (Cooked weight)           | -     | -     | 21    | 30    |
| Carrot (Cooked weight)          | 42    | 49    | -     | 22    |
| Tocopherol                      | 300mg | -     | 300mg | 300mg |
| Beetroot puree (50%)            | 20    | 20    | 12    | 10    |
| Sugar beet fibre                |       |       | 18    |       |
| Guar gum powder                 | 0.5   | 0.5   | 0.5   | 0.5   |
| Acetic acid                     | 1.0   |       |       |       |
| Malic acid                      | 1.0   |       |       |       |
| Citric acid                     | -     | 3.0   | 2.0   | 1.0   |
| Ascorbic acid                   |       |       | 1.0   | 1.0   |
| Benzoic acid                    | 300mg | 300mg | 300mg | 300mg |
| Sorbic acid                     | 300mg | 300mg | 300mg | 300mg |
| Anchovy paste                   | 15    | -     | 20    | 30    |
| Blended fish oil (18% w/w EPA)  | 50    | -     | -     | -     |
| Sardine oil (28% w/w EPA)       | -     | -     | -     | 35    |
| Smoked salmon (commminuted)     | -     | 10    | -     | -     |
| Salmon oil                      | -     | 100   | -     | -     |
| Cod liver oil                   | -     | -     | 100   | -     |
| Evening primrose oil            |       |       |       | 12    |
| Sunflower oil                   | 50    | -     | -     | 48    |
| Ground peanuts                  | -     | -     | 10    | -     |

Each of the examples 1-4 are smooth or granular emulsified pastes of a soft consistency and the flavours of the pastes are reminiscent of smoked salmon, prawn cocktail or other fish flavours.

The invention can also yield compositions according to the invention which are flavoured with essential oils to mask the flavour of the fish oil, as illustrated by the following examples.

Examples 5&6

Quantities in g unless otherwise stated, batch size 300g.

|                                | 5     | 6     |       |       |
|--------------------------------|-------|-------|-------|-------|
| Split peas (Cooked weight)     | 102.6 | 90    | 90    | 20    |
| Soy bean flour (defatted)      |       | 30    | 40    | 40    |
| Red Lentils                    | -     | 10    |       |       |
| Egg Yolk                       |       | 7     |       |       |
| AL 721 (fractionated egg yolk) | 90    |       |       | 90    |
| Onion (Cooked weight)          | 50    | -     | 20    | 20    |
| Carrot (Cooked weight)         | 50    | 36    | 25    | 15    |
| Tomato puree                   | -     | 30    |       | 45mg  |
| Tocopherol                     | 300mg | 300mg | 300mg | 300mg |
| Curry powder (mild Madras)     | 3     | -     | 10    | 10    |
| Oil of thyme                   | -     | 0.1   |       |       |
| Oil of sage                    | -     | 0.1   |       |       |
| Activated charcoal             |       |       | 60    |       |
| Guar gum                       | 0.5   | 3.0   |       | 0.5   |
| Xanthan gum                    |       |       | 1.0   |       |
| Acetic Acid                    | 1.0   |       | 1.0   |       |
| Ascorbic Acid                  | 1.0   | 1.0   | 1.0   | 1.0   |
| Citric Acid                    | 1.0   | 1.0   |       | 1.0   |
| Malic Acid                     |       | 1.0   | 1.0   | 1.0   |
| Benzoic acid                   | 300mg | 300mg | 300mg | 300mg |
| Sorbic acid                    | 300mg | 300mg | 300mg | 300mg |
| Fish oil (18% w/w EPA)         |       | -     | 50    |       |
| Cod liver oil (9% w/w EPA)     | -     | 100   |       | 100   |

The required quantity of cooked vegetable is weighed into a blender, tocopherol added and a puree prepared. The other ingredients are added in order; the fish oil is added and the acid added last of all. Blending is continued until a homogeneous paste is produced.

A variety of flavours can also be produced by substitution of other root vegetables, for example potato, parsnip, celeriac or swede for a proportion of the carrot and onion.

The nutritional composition may be packed in unit dose packs of from 15-250g. The unit dose packs may be made from metal foil or plastic material and hermetically sealed with a metallic, plastic or laminated foil. The composition may also be packed in commercially available containers with a resealable closure.

## CLAIMS

1. A nutritional or medicinal composition in the form of a paste containing oil which provides at least one essential polyunsaturated fatty acid, and dietary fibre.
2. A composition as claimed in claim 1, wherein the essential fatty acids are derived from fish oil.
3. A composition as claimed in claim 1 wherein the essential fatty acids are eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA) and/or linolenic acid.
4. A composition as claimed in any one of the preceding claims wherein the content of EPA is between 0.3 - 3.6g and the content of linolenic acid is between 0.1-2 g and the content of dietary fibre is 2.0-5.0g per portion or serving of 30-100g.
5. A composition as claimed in any one of the preceding claims wherein at least 5% of the dietary fibre is derived from leguminous seeds and/or edible roots, tubers and nuts which contain an emulsifying agent.
6. A composition as claimed in any one of the preceding claims wherein there is also present an emulsifying agent.
7. A composition as claimed in any of the preceding claims containing activated charcoal, cholestyramine or another agent capable of sequestering bile acids.
8. A composition as claimed in any of the preceding claims wherein egg yolk or solvent extract of egg yolk provides the essential fatty acid and emulsifying agent.
9. A composition as claimed in any of the preceding claims wherein the essential fatty acids are provided by fresh or smoked fish, marine animals, fish liver oil, fish body oil, vegetable oil or a blend thereof.

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10. A composition as claimed in any of the preceding claims containing one or more antimicrobial preservatives and one or more antioxidants.
11. A composition as claimed in any one of the preceding claims wherein the paste is flavoured and coloured with naturally occurring agents.
12. A composition as claimed in any one of the preceding claims comprising a quantity of fish oil such that it provides at least 0.3 g of EPA in a hermetically sealed unit dose container from which air has been excluded.
13. A composition as claimed in claim 1 and substantially as hereinbefore described in any one of the examples.

Amendments to the claims  
have been filed as follows

1. A nutritional or medicinal composition adapted for oral administration to humans, said composition being in the form of an oil-containing paste comprising at least one omega-3 polyunsaturated fatty acid (w-3 PUFA), said composition containing 0.6 to 3.6g of w-3 PUFA and 1.0g to 8.0g of cooked dietary fibre per 30 to 100g of the composition.
2. A composition as claimed in claim 1, wherein the w-3 PUFA is provided in the form of a fish liver oil or fish body oil which contains eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA) and which has been processed to reduce the amount of vitamins A & D.
3. A composition as claimed in claim 1 or claim 2 wherein the w-3 PUFA and dietary fibre are present in a ratio such that when the composition is divided into individual portions of 30 - 100g there are 0.25g to 1.5g of w-3 PUFA and 1.0 to 8.0g of dietary fibre, and wherein at least 5% of the dietary fibre is derived from at least one of a leguminous seed, and edible root, tuber and nut which also contain an emulsifying agent.
4. A composition as claimed in any one of the preceding claims wherein there is also present a non-vegetable emulsifying agent.
5. A composition as claimed in claim 4 wherein egg yolk or solvent extract of egg yolk provides the emulsifying agent.
6. A composition as claimed in any one of the preceding claims containing activated charcoal, cholestyramine or another agent capable of sequestering bile acids.
7. A composition as claimed in any one of the preceding claims which comprises fresh or smoked fish, or flesh from a marine animal, or a blend thereof.
8. A composition as claimed in any of the preceding claims containing one or more antimicrobial preservatives and one or more antioxidants.
9. A composition as claimed in any of the preceding claims wherein the paste is flavoured and coloured with naturally occurring agents.
10. A composition as claimed in any of the preceding claims which provides at least 0.3g of EPA in a hermetically sealed unit dose container from which air has been excluded.
11. A composition as claimed in claim 1 and substantially as hereinbefore described in any one of the examples.